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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|------------------------|---------------------|------------------|
| 09/465,429 | 12/21/1999 | RICHARD C. BOUCHER JR. | 5470-250 | 8856 |

20792 7590 12/31/2003

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RALEIGH, NC 27627

EXAMINER

WANG, SHENGJUN

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1617

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/465,429

Applicant(s)

BOUCHER, RICHARD C.

Examiner

Shengjun Wang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on October 3 & 22, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-24, 31, 32, 37, 44, 49 and 51-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-24, 31, 32, 37, 44, 49 and 51-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 19.
- 4) ☒ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 3, 2003 and the supplemental submission filed on October 22, 2003 has been entered.

Applicants' election in paper No. 12 is presumed to carry over to the instant RCE since applicants have not indicated a contrary intention. The claims have been examined insofar as they read on elected species.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 22-24,31,32,37,44,49,51-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson (IDS, 5) in view of Boucher, Jr. et al. (U.S. Patent 5,876,700) and Jungherr et al. (U.S. Patent 5,837,266), and in further view of Robison et al. (IDS, October 3, 2003) and Eng et al. (IDS, October 3, 2003).

3. Anderson teaches a method of increasing mucociliary clearance or inducing sputum comprising the step of causing a subject to inhale into subject's airway an osmolyte to increase

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the osmolarity of airway surface liquid. See, particularly, claims 12-21. The osmolyte may be any substance that is biologically compatible with the subject, preferably mineral salts, and more preferably sodium and potassium salt. See, column 3, lines 12-25, and claims 15 and 16. The technique, i.e., increasing mucociliary clearance and inducing sputum, is known to be useful for subject having cystic fibrosis. See, column 2, lines 14-33. Anderson further suggest the employment of aerosol administration for inhalation. See, particularly, col. 2, lines 14-33 in Anderson et al.

4. Anderson does not teach expressly the employment of the method for treating cystic fibrosis, or administering a sodium channel blocker agent with an osmolyte for treating cystic fibrosis, or employ potassium sulfate as the osmolyte.

5. However, Boucher, Jr. et al. teach a method for hydrating mucous secretions in lungs, or for treating cystic fibrosis comprising administering to the patient by inhalation benzaminil or phenamil, the sodium channel blocker employed herein. See, particularly, the abstract, claims 1-5, 7-10, and 12-16. Jungherr et al. teaches that potassium sulfate is known to be biological compatible with human and is known to be useful in therapeutical composition as osmolyte. See, particularly, column 3, lines 26-33. Further, Eng teaches specifically the usefulness of osmolyte (as hypertonic solution) in mucociliary clearance and in providing treatment of cystic fibrosis. See particularly, the abstract, the introduction and discussion in Eng. Robinsons further teaches the usefulness of hypertonic saline in combination with amiloride, an sodium channel blocking agent. See, particularly, the abstract, and the discussion.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to treat a subject with cystic fibrosis by

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administering to the subject a combination of osmolyte, such as potassium sulfate and a sodium channel blocker, such as benzaminil or phenamil.

A person of ordinary skill in the art would have been motivated to treat a subject with cystic fibrosis by administering to the subject a combination of osmolyte, such as potassium sulfate and a sodium channel blocker, such as benzaminil or phenamil because it is prima facie obvious to combine two agents each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus , the claimed invention which is drawn to a method for treating cystic fibrosis employing a combination of two agents, each of them is known to be useful for treating cystic fibrosis, sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. The combination herein is obvious also because of the fact that hypertonic solution is known to provide benefit for treating cystic fibrosis when combined with other known anti-cystic fibrosis agent. The employment of potassium sulfate is seen to be a selection from amongst equally suitable potassium salts, particularly because potassium sulfate is known to be biological compatible to human and is known to be used as osmolyte in therapeutical composition. Ex parte Winters 11 USPQ 2nd 1387 (at 1388).

Response to the Arguments

Applicants' amendments and remarks submitted October 22, 2003 have been fully considered, but are not persuasive, particularly because of the new ground rejections set forth above.

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Specifically, Robinson and Eng provide further evidence that using osmotically active agent for increasing mucociliary clearance or inducing sputum is a known method for treating cystic fibrosis.

The remarks and the exhibits that the instant claims provide enhanced drug penetration have been considered, but are not persuasive to overcome the rejection set forth above. As discussed above, a prima facie case for employing a combination of cystic fibrosis treating agent and osmotically active agent have been established. An unexpected result has to be established to rebut the rejection. Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be unexpected and significant. See MPEP 716.02 (b). The claims must be commensurate in the scope with any evidence of unexpected results. See MPEP 716.02 (d). Further, A DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case if obviousness. See, MPEP 716.02 (e).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang, Ph.D. whose telephone number is (703) 308-4554. The examiner can normally be reached on Monday-Friday from 8:30 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (703) 305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Primary Examiner

Shengjun Wang

December 22, 2003